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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/417,268	10/13/99	CHENCHIK	A	CLON-008

HM12/0405

BRET FIELD
BOZICEVIC FIELD & FRANCIS LLP
200 MIDDLEFIELD ROAD
SUITE 200
MENLO PARK CA 94025

EXAMINER
FORMAN, B

ART UNIT	PAPER NUMBER
1655	19

DATE MAILED: 04/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

CTNF

Office Action Summary	Application No.	Applicant(s)	
	09/417,268	CHENCHIK, ALEX	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,53 and 57-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 53 57-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 16 March 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/417,268 is acceptable and a CPA has been established. An action on the CPA follows.

Papers filed 16 March 2001 in Paper No. 17 in which claims 1, 12, 57 & 58 were amended and new claims 60-77 were added is acknowledged. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 10 dated 16 October 2000 are maintained. All of the arguments have been thoroughly reviewed and are discussed below. New grounds for rejection are discussed.

Currently claims 1-17, 53, 57-77 are under prosecution.

Claim Rejections - 35 USC § 112

2. Claims 1-17, 53 & 60-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 1-17, 53 & 60-77 are indefinite in Claims 1 & 60 for the recitation "stably associated with" because "stably" is a relative term that requires definition or criteria for determining and because "associated with" is a non-specific relational phrase and therefore the relationship between the "spots" and the "support" is not defined. It is suggested that Claims 1 & 60 be amended to define or recite criteria for determining "stably" and to define the relationship between the "spots" and "support" e.g. replace "stably associated with" with "attached to".

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 5-10, 12-17, 57 & 58 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1995).

Regarding Claim 1, Brown et al. disclose an array which is a multi-cell substrate, comprising at least one pattern of probe oligonucleotide spots wherein a spot is a "cell" on a multi-cell substrate wherein each "cell" contains a microarray, wherein the spots (microarrays) are attached to the surface of a solid support (Column 11, lines 43-67), wherein each probe oligonucleotide spot (microarray) comprises a plurality of unique oligonucleotides (Column 4, lines 16-19) wherein said plurality comprises 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid i.e. all known mutations (different sequence) of a given gene (target nucleic acid (Column 15, lines 22-27).

Regarding Claim 2, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein said plurality of unique oligonucleotides hybridize to different regions of the target nucleic acid wherein the different regions represent all known mutations in a disease gene (Column 15, lines 19-27).

Regarding Claim 5, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein two or more different target nucleic acids are represented in said pattern (Column 4, lines 52-55).

Regarding Claim 6, Brown et al. disclose the array (multi-cell substrate) wherein each oligonucleotide spot (microarray) corresponds to a different target nucleic acid i.e. different target yeast nucleic acids are arrayed in different spots (microarrays) of the array (Example 3, Column 18, lines 39-43).

Regarding Claim 7, Brown et al. disclose the array (multi-cell substrate) of Claim 5 wherein two or more oligonucleotide spots (microarray) correspond to the same target nucleic acid (Column 13, lines 1-10).

Regarding Claim 8, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein said array comprises a plurality of said patterns of oligonucleotide spots (microarray) (Column 11, lines 51-58).

Regarding Claim 9, Brown et al. disclose the array (multi-cell substrate) of Claim 8 wherein said plurality of patterns are separated from each other by walls which are grids (Column 4, lines 45-51).

Regarding Claim 10, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein each of said oligonucleotides range from 15 to 150 nucleotides in length (Column 13, lines 21-22).

Regarding Claim 12, Brown et al. teach the array (multi-cell substrate) of Claim 1 wherein the oligonucleotide probe composition comprises about 3 to 50 oligonucleotides i.e. each oligonucleotide probe spot (microarray) has a size of $1mm^2$ (Column 11, line 62-67) and a probe density of 100 per cm^2 (Column 6, lines 32-33).

Regarding Claim 13, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein all of the oligonucleotide spots hybridize to the same type of target nucleic acid i.e. cDNA (Column 4, lines 60-64).

Regarding Claim 14, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein the density of spots (microarray) on said array does not exceed about $1000/cm^2$ (Column 11, lines 62-67).

Regarding Claim 15, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein the density of spots (microarray) on said array does not exceed about $400/cm^2$ (Column 11, 62-67).

Regarding Claim 16, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein the number of spots (microarray) on said array ranges from about 50 to 10,000 i.e. 96 (Column 11, 62-67).

Regarding Claim 17, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein the number of spots (microarray) on said array ranges from about 50 to 1,000 i.e. 96 (Column 11, 62-67).

Regarding Claim 57, Brown et al. teaches an array which is a multi-cell substrate, comprising a pattern of probe oligonucleotide spots which are microarrays, that are attached to a surface of a solid support (Column 11, lines 51-61) wherein each probe oligonucleotide spot (microarray) comprises an oligonucleotide probe composition comprising of 3 to 50 unique oligonucleotides (Column 6, lines 32-33 and Column 11, line 62-67) of from about 15 to 150 nucleotides in length (Column 13, lines 21-22) and wherein each unique oligonucleotide hybridizes to a different region of the target nucleic acid (Example 3, Column 18, lines 40-43).

Regarding Claim 58, Brown et al. teaches an array which is a multi-cell substrate, comprising a pattern of probe oligonucleotide spots which are microarrays, that have a density that does not exceed about 400 spots (microarray)/cm^2 attached to a surface of a solid support (Column 11, lines 62-67) wherein each probe oligonucleotide spot (microarray) corresponds to a different target nucleic acid (Example 3, Column 18, lines 40-43) and comprises an oligonucleotide composition consisting of 3 o 20 unique oligonucleotides (Column 6, lines 32-33 and Column 11, line 62-67) of from about 25 to 100 nucleotides in length (Column 13, lines 21-22) wherein each unique oligonucleotide hybridizes to a different region of the target nucleic acid (Example 3, Column 18, lines 40-43).

Response to Arguments

6. Applicant argues that the examiner incorrectly equates the instantly claimed spots with the cells in the multi-cell array of Brown et al. because, in view of the specification which discloses array embodiments that are made of a plurality of oligonucleotide spot patterns, the instantly claimed "probe spots" are equal to the regions not the cells in the multi-cell array of Brown et al. In response to applicant's argument that the references fail to show certain

features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a plurality of spot patterns) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Additionally, the argument is not found persuasive because the instantly claimed probe spot, as claimed, is disclosed by Brown et al. i.e. each cell of the multi-cell array comprises a microarray (Column 11, lines 55-58) is stably associated with the surface of a solid support, consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid (Column 13, lines 1-10).

Applicant argues that the probes of Brown et al. are positioned at a defined location and not present as a mixture. This argument is not found persuasive because the limitation "mixture" does not define or limit the location of the probes on the array.

Applicant further argues that one of skill in the art would not interpret the Brown et al. cell as comprising probes that hybridize to different targets and not the same target as claimed. This argument is not found persuasive because Brown et al. specifically teaches and embodiments wherein the probes hybridize to the same target i.e. "all known mutations of a given gene" (Column 15, lines 22-27).

7. Claims 1-3, 5-8, 13-17, 53 & 59 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Pinkel et al. (U.S. Patent No. 5,830,645, filed 9 December 1994).

Regarding Claim 1, Pinkel et al. disclose an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence (i.e. restriction enzyme digested genomic sequences) that hybridize to the same target nucleic acid (i.e. one probe spot consists of a plurality of unique sequences that hybridize to cMYC and a second probe spot consists of a plurality of unique sequences that hybridize to 21D7 region of the human genome) (Example 1, Column 13-14).

Regarding Claim 2, Pinkel et al. disclose the array wherein said plurality of unique oligonucleotides hybridize to different regions of said target nucleic acid i.e. target fragments of different size hybridize to different regions of the target (Column 13, lines 10-18)

Regarding Claim 3, Pinkel et al. disclose the array wherein said plurality of unique oligonucleotides hybridize to non-overlapping region of said target i.e. the DNA is digested to completion with restriction enzyme (Column 13, lines 15-18).

Regarding Claim 5, Pinkel et al. disclose the array wherein two different target nucleic acids are represented in said pattern i.e. cMYC and 21D7 (Column 13, lines 10-18).

Regarding Claim 6, Pinkel et al. disclose the array wherein each oligonucleotide spot corresponds to a different target nucleic acid i.e. anonymous clones (Column 4, lines 19-23).

Regarding Claim 7, Pinkel et al. disclose the array wherein two or more oligonucleotide spots correspond to the same target nucleic acid i.e. cMYC and 21D7 (Column 13, lines 10-18 and Fig. 1).

Regarding Claim 8, Pinkel et al. disclose the array wherein said array comprises a plurality of said patterns of oligonucleotide spots (Fig. 1).

Regarding Claim 13, Pinkel et al. disclose the array wherein all of the oligonucleotide spots hybridize to the same type of target nucleic acid i.e. human genomic (Column 13, lines 10-18).

Regarding Claim 14, Pinkel et al. disclose the array wherein the density of spots does not exceed about 1000/cm^2 (Column 4, lines 6-29).

Regarding Claim 15, Pinkel et al. disclose the array wherein the density of spots does not exceed about 400/cm^2 (Column 4, lines 6-29).

Regarding Claim 16, Pinkel et al. disclose the array wherein the number of spots on said array ranges from about 50 to 10,000 i.e. 96 (Column 4, lines 24-29).

Regarding Claim 17, Pinkel et al. disclose the array wherein the number of spots on said array ranges from about 50 to 1,000 i.e. 96 (Column 4, lines 24-29).

Regarding Claim 53, Pinkel et al. disclose a kit for use in a hybridization assay, said kit comprising an array according to Claim 1 (Column 3, lines 42-50).

Regarding Claim 59, Pinkel et al. disclose the kit further comprising reagents for generating a labeled target nucleic acid sample (Column 3, lines 47-50).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 3-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1995) as applied to claim 1 above, and further in view of Fodor et al. (U.S. Patent No. 5,800,992, filed 25 June 1996).

Regarding Claim 3, Brown et al. disclose the array (multi-cell substrate) of Claim 1 comprising at least one pattern of probe oligonucleotide spots (microarray) attached to a surface of a solid support wherein each oligonucleotide spot (microarray) comprises a plurality of unique oligonucleotides for a target nucleic acid. Additionally, Brown et al. teach the unique oligonucleotides are positioned at known addressable regions (Column 11, lines 55-58) and hybridize to all known mutations in a disease gene (Column 15, lines 19-22). Brown et al. do not teach said plurality of unique oligonucleotides hybridize to non-overlapping regions of said target nucleic acid. However, Fodor et al. teach a similar microarray comprising a pattern of unique oligonucleotide probes attached to a surface of a solid support wherein the probes are attached to the support in a matrix of positionally defined regions (Column 2, lines 34-40) and wherein the oligonucleotide probes for fingerprinting hybridize with "absolute complementary matching" to the target sequence (Column 9, lines 60-67).

Regarding Claim 4, Brown et al. do not teach said plurality of unique oligonucleotides hybridize to overlapping regions of said target nucleic acid. However, Fodor et al. teach a similar microarray wherein the oligonucleotide probes for mapping hybridize to overlapping regions of a target nucleic acid (Column 10, lines 1-12). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Brown et al. with the teaching of Fodor et al. to obtain the claimed invention because one of skill in the art would have been motivated with a reasonable expectation of success to modify the oligonucleotide probes of Brown et al. with the oligonucleotide probes of Fodor et al. wherein both sets of probes are used in hybridization assays, based on the oligonucleotide probes' equivalent chemical and physical properties and the oligonucleotide probes' equivalent positioning on the substrate and based on experimental design wherein overlapping probes are used for mapping and non-overlapping probes are used for fingerprinting for the expected benefit of rapid and convenient screening, eliminating the need to handle and detect individual arrays as taught by Brown et al. (Column 15, lines 59-64).

Response to Arguments

10. Applicant argues that Brown et al. fail to teach the claimed array in which each probe spot includes two or more different oligonucleotides of different sequence that hybridize to the same target nucleic acid and that the teaching of Fodor et al. fails to make up the deficiency of Brown et al. because Fodor et al. teach different target sequences. This argument is not found persuasive because Fodor et al. clearly teaches probes compositions that hybridize to the same target (Column 32, lines 12-24) wherein the probes are different and non-overlapping (Column 32, lines 12-14) or overlapping (Column 32, lines 25-28). Applicant argues that the combination of Brown et al. and Fodor et al. do not teach or suggest the claimed invention. This argument is not found persuasive because as stated above, Brown et al. teach the claimed array comprising two or more different oligonucleotides of different sequence that hybridize to the same target nucleic acid and Fodor et al. teach arrays comprising overlapping and non-overlapping probes which hybridize to the same target.

11. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1995) as applied to Claim 1 and further in view of Lockhart et al. (U.S. Patent No. 6,040,138, filed 15 September 1995).

Regarding Claim 11, Brown et al. do not teach the array (multi-cell substrate) of Claim 1 wherein the array further comprises at least one mismatch probe. However, Lockhart et al. teach a similar microarray comprising a pattern of unique oligonucleotide probes attached to a surface of a solid support wherein the probes are attached to the support in a matrix of positionally defined regions (Column 2, lines 60-65) and wherein the microarray comprises at least one mismatch probe (Column 3, line 30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the microarray of Brown et al. to include mismatch control probes as taught by Lockhart et al. wherein hybridization signal intensity is compared to mismatch hybridization for the expected benefit of accurately quantifying hybridization as taught by Lockhart et al. (Column 3, lines 30-38).

Response to Arguments

12. Applicant argues that Brown et al. fail to teach an array on which each probe spot includes two or more different oligonucleotides of different sequence that hybridize to the same target nucleic acid and that the teaching of Lockhart et al. fails to make up the deficiency of Brown et al. such that the combined teachings fail to teach or suggest the claimed probe composition. This argument is not found persuasive because as cited above, Brown et al. clearly discloses the claimed probe spot composition (Column 15, lines 19-27).

13. Claims 53 & 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1995) in view of Stratagene catalog (1989, page 39).

Regarding Claim 53, Brown et al. teach the array of Claim 1 comprising at least one pattern of probe oligonucleotide spots which are microarrays are attached to a surface of a solid support wherein each oligonucleotide spot (microarray) comprises a plurality of unique

oligonucleotides for a target nucleic acid. Additionally, they teach hybridization assay and assay reagents wherein the assay is performed on said array (Example 3, Column 18, lines 34-63). Brown et al. do not teach the combined into a kit. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

Regarding Claim 59, Brown et al. teach the hybridization assay further comprising reagents for generating a labeled target nucleic acid sample (Column 16, lines 39-54). Brown et al. do not teach the combined into a kit. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Brown et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

Response to Arguments

14. Applicant argues that Brown et al. fail to teach an array on which each probe spot includes two or more different oligonucleotides of different sequence that hybridize to the same target nucleic acid and that the motivation to combine reagents into a kit taught by Stratagene fails to make up the deficiency of Brown et al. such that the combined teachings fail to teach or suggest the claimed kit. This argument is not found persuasive because as cited above, Brown et al. clearly discloses the claimed probe spot composition (Column 15, lines 19-27).

15. Claims 4, 9-10, 12, 57 & 58 are rejected under 35 U.S.C. 103(a) as obvious over Pinkel et al. 5,830,645, filed 9 December 1994).

Regarding Claim 4, Pinkel et al. teach the array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of

different sequence that hybridize to the same target nucleic acid (Example 1, Column 13-14) wherein the unique oligonucleotides comprise restriction digested DNA fragments (Column 13, lines 15-18) but they do not teach the fragments hybridized to overlapping regions of said target. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the complete digestion of Pinkel et al. with a partial digestion to thereby provide fragments which hybridize to overlapping regions for the known benefit of mapping the target by analyzing overlapping hybridizations.

Regarding Claim 9, Pinkel et al. teach the spots are arrayed for individual detection by optimizing spot size and substrate material etc. (Column 8, lines 31-40) do not teach said plurality of patterns are separated from each other by walls. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrayed spots of Pinkel et al. by separating the spots from each other by walls for the obvious benefit of physically separating the spots by walls to thereby facilitate individual detection.

Regarding Claim 10, Pinkel et al. teach said oligonucleotides may be of different length wherein the length is not critical to the invention (Column 4, lines 36-40) but they do not teach each of said oligonucleotides range from 15 to 150 nucleotides in length. However, probes of 15 to 150 nucleotides were well known in the art at the time the claimed invention was made and it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the oligonucleotide length of Pinkel et al. with oligonucleotides of 15 to 150 nucleotides for the known benefit of increased selectivity of short probes.

Regarding Claim 12, Pinkel et al. do not teach the plurality of probes ranges from 3 to 50 oligonucleotides. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe spots of Pinkel et al. to comprise a mixture of 3 to 50 unique oligonucleotides for the obvious benefit of optimizing experimental conditions to maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105

USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 57, Pinkel et al. teach an array comprising a pattern of probe oligonucleotide spots wherein each probe spot comprises an oligonucleotide probe composition consisting of unique oligonucleotides of different sequence that hybridize to the same target nucleic acid wherein each oligonucleotide hybridizes to a different region of said target nucleic (Example 1, Column 13, lines 1-32) but they do not teach the probe mixture consists of a mixture of 3 to 50 oligonucleotides from about 15 to 150 nucleotides in length. However, probe lengths of 15 to 150 nucleotides were well known in the art at the time the claimed invention was made and it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the oligonucleotide length of Pinkel et al. with oligonucleotides of 15 to 150 nucleotides for the known benefit of increased selectivity of short probes. The skilled practitioner in the art would have been further motivated to modify the probe spots of Pinkel et al. to comprise a mixture of 3 to 50 unique oligonucleotides for the obvious benefit of optimizing experimental conditions to maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 58, Pinkel et al. teach an array comprising a pattern of probe oligonucleotide spots of a density that does not exceed about 400 spots/cm^2 wherein each probe spot consists of a mixture of unique oligonucleotides of different sequence that hybridize to the same target nucleic acid wherein each unique oligonucleotide hybridizes to a different region of said target (Example 1, Column 13, lines 1-32) but they do not teach the mixture of 3 to 20 unique oligonucleotides from about 25 to 100 nucleotides in length. However, probe lengths of 25 to 100 nucleotides were well known in the art at the time the claimed invention was made and it would have been obvious to one of ordinary skill in the art at the time the

claimed invention was made to modify the oligonucleotide length of Pinkel et al. with oligonucleotides of 25 to 100 nucleotides for the known benefit of increased selectivity of short probes. The skilled practitioner in the art would have been further motivated to modify the probe spots of Pinkel et al. to comprise a mixture of 3 to 20 unique oligonucleotides for the obvious benefit of optimizing experimental conditions to maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

16. Claims 11 & 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al. (U.S. Patent No. 5,830,645, filed 9 December 1994) in view of Lockhart et al. (U.S. Patent No. 6,040,138, filed 15 September 1995).

Regarding Claim 11, Pinkel et al. teach an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid (Example 1, Column 13-14) but they do not teach the array further comprises at least one mismatch probe.

Regarding Claim 70, Pinkel et al. teach an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support wherein each probe spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridized to the same target nucleic acid (Example 1, Column 13, lines 10-15) but they do not teach the array further comprises at least one mismatch probe. However, Lockhart et al. teach a similar array comprising a pattern of unique oligonucleotide probes attached to a surface of a solid support wherein the probes are attached to the support in a

matrix of positionally defined regions (Column 2, lines 60-65) and wherein the microarray comprises at least one mismatch probe (Column 3, line 30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrays of Pinkel et al. to include mismatch control probes as taught by Lockhart et al. wherein hybridization signal intensity is compared to mismatch hybridization for the expected benefit of accurately quantifying hybridization as taught by Lockhart et al. (Column 3, lines 30-38).

17. Claims 60-69 & 71-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al. (U.S. Patent No. 5,830,645, filed 9 December 1994) in view of Lapidus et al. (U.S. Patent No. 6,146,828, filed 3 July 1998).

Regarding Claim 60, Pinkel et al. teach an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support wherein each probe spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridized to the same target nucleic acid (Example 1, Column 13, lines 10-15) but they do not teach the oligonucleotides of different sequence cooperatively hybridize to the same target. However, cooperative hybridization was well known in the art at the time the claimed invention was made and it was known in the art that cooperatively hybridizing oligonucleotide probes provide increased selectivity and increased stability compared to longer contiguous probes as taught by Lapidus et al. (Column 9, line 53-Column 10, line 7). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the longer probes of Pinkel et al. with the shorter, cooperatively hybridizing probes as taught by Lapidus et al. for the expected benefit of providing an array of probes having increased selectivity and increased stability (Lapidus, Column 9, line 53-Column 10, line 7).

Regarding Claim 61, Pinkel et al. teach the array wherein said plurality of unique oligonucleotides hybridize to different regions of said target nucleic acid i.e. target fragments of different size hybridize to different regions of the target (Column 13, lines 10-18)

Regarding Claim 62, Pinkel et al. teach the array wherein said plurality of unique oligonucleotides hybridize to non-overlapping region of said target i.e. the DNA is digested to completion with restriction enzyme (Column 13, lines 15-18).

Regarding Claim 63, Pinkel et al. teach the array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid (Example 1, Column 13-14) wherein the unique oligonucleotides comprise restriction digested DNA fragments (Column 13, lines 15-18) but they do not teach the fragments hybridized to overlapping regions of said target. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the complete digestion of Pinkel et al. with a partial digestion to thereby provide fragments which hybridize to overlapping regions for the known benefit of mapping the target by analyzing overlapping hybridizations.

Regarding Claim 64, Pinkel et al. teach the array wherein two different target nucleic acids are represented in said pattern i.e. cMYC and 21D7 (Column 13, lines 10-18).

Regarding Claim 65, Pinkel et al. teach the array wherein each oligonucleotide spot corresponds to a different target nucleic acid i.e. anonymous clones (Column 4, lines 19-23).

Regarding Claim 66, Pinkel et al. teach the array wherein two or more oligonucleotide spots correspond to the same target nucleic acid i.e. cMYC and 21D7 (Column 13, lines 10-18 and Fig. 1).

Regarding Claim 67, Pinkel et al. teach the array wherein said array comprises a plurality of said patterns of oligonucleotide spots (Fig. 1).

Regarding Claim 68, Pinkel et al. teach the spots are arrayed for individual detection by optimizing spot size and substrate material etc. (Column 8, lines 31-40) do not teach said plurality of patterns are separated from each other by walls. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrayed spots of Pinkel et al. by separating the spots from each other by walls for the obvious benefit of physically separating the spots by walls to thereby facilitate individual detection.

Regarding Claim 69, Pinkel et al. teach said oligonucleotides may be of different length wherein the length is not critical to the invention (Column 4, lines 36-40) but they do not teach each of said oligonucleotides range from 15 to 150 nucleotides in length. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the oligonucleotide length of Pinkel et al. with oligonucleotides of 15 to 150 nucleotides for the known benefit of increased selectivity of short probes (Lapidus, Column 9, line 53-Column 10, line 7).

Regarding Claim 71, Pinkel et al. do not teach the plurality of probes ranges from 3 to 50 oligonucleotides. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe spots of Pinkel et al. to comprise a mixture of 3 to 50 unique oligonucleotides for the obvious benefit of optimizing experimental conditions to maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 72, Pinkel et al. teach the array wherein all of the oligonucleotide spots hybridize to the same type of target nucleic acid i.e. human genomic (Column 13, lines 10-18).

Regarding Claim 73, Pinkel et al. teach the array wherein the density of spots does not exceed about 1000/cm^2 (Column 4, lines 6-29).

Regarding Claim 74, Pinkel et al. teach the array wherein the density of spots does not exceed about 400/cm^2 (Column 4, lines 6-29).

Regarding Claim 75, Pinkel et al. teach the array wherein the number of spots on said array ranges from about 50 to 10,000 i.e. 96 (Column 4, lines 24-29).

Regarding Claim 76, Pinkel et al. teach the array wherein the number of spots on said array ranges from about 50 to 1,000 i.e. 96 (Column 4, lines 24-29).

Regarding Claim 77, Pinkel et al. teach a kit for use in a hybridization assay, said kit comprising an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support wherein each probe spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridized to the same target nucleic acid (Example 1, Column 13, lines 10-15) but they do not teach the oligonucleotides of different sequence cooperatively hybridize to the same target. However, cooperative hybridization was well known in the art at the time the claimed invention was made and it was known in the art that cooperatively hybridizing oligonucleotide probes provide increased selectivity and increased stability compared to longer contiguous probes as taught by Lapidus et al. (Column 9, line 53-Column 10, line 7). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the longer probes of Pinkel et al. with the shorter, cooperatively hybridizing probes as taught by Lapidus et al. for the expected benefit of providing an array of probes having increased selectivity and increased stability (Lapidus, Column 9, line 53-Column 10, line 7).

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re*

Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-8, 14-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,077,673. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are generic over the patent species and a genus is always obvious over the species. Therefore, the instant claims are obvious over the patent claims.

20. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

21. Claim 10 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of copending Application No. 09/440,829. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

22. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. Claims 1-17 & 53 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 & 35 of copending Application No. 09/440,829. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support wherein they differ only in the '829 claims recite "high hybridization efficiency" and "low propensity for non-specific hybridization". However, the instant target-specific probes i.e. which hybridize to different regions of the target (Claim 2), which hybridize to non-overlapping regions of a target (Claim 3), and unique oligonucleotides which hybridize to overlapping regions of a target (Claim 4) is not patentably distinct from the '829 probe-target hybridization efficiency and specificity because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made that the instant probe-target specificity would provide the '829 recited "high hybridization efficiency" and "low propensity for non-specific hybridization".

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

24. No claim is allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this

application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
April 3, 2001

S. Forman